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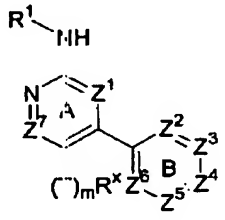
Applicants: Mark Ledeboer et al.
Application No.: 10/700,333

AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

1. (Currently amended) A compound of formula **I**:



I

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is a phenyl, cyclohexyl, cyclopentyl, pyridyl, morpholino, piperazinyl, or piperidinyl group, wherein R^1 ~~$Q\text{-}Ar^t$~~;

~~Q is a C_{1-3} alkylidene chain wherein one methylene unit of Q is optionally replaced by O, NR, NRCO, NRCONR, $NRCO_2$, CO, CO_2, CONR, OC(O)NR, SO_2, SO_2NR, $NRSO_2$, $NRSO_2NR$, C(O)C(O), or $C(O)CH_2C(O)$;~~

~~Ar^t is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar^t~~ is optionally substituted with q independent occurrences of $Z\text{-}R^Z$; wherein q is 0-5, Z is a bond or is a C_1-C_6 alkylidene chain wherein up to two non-adjacent methylene units of Z are optionally and independently replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR; and each occurrence of R^Z is independently selected from R', halogen, NO_2, CN, OR', SR', $N(R')_2$, NR'COR', $NR'CON(R')_2$,

$NR'CO_2R'$, COR', CO_2R', $OCOR'$, $CON(R')_2$, $OCON(R')_2$, SOR', SO_2R', $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, $COCOR'$, or $COCH_2COR'$;

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Z^1 is N;

Z^7 is $C(U)_nR^Y$;

T and U are each independently a bond or a saturated or unsaturated C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR;

m and n are each independently 0 or 1;

R^X and R^Y are each independently selected from R or Ar^1;

Z^2 is N or CR^2; Z^3 is N or CR^3; Z^4 is N or CR^4; Z^5 is N or CR^5; and Z^6 is N or CR^6, wherein each occurrence of R^2, R^3, R^4, R^5 or R^6 is independently R^U or $(V)_pR^V$, provided that a) no more than three of Z^2, Z^3, Z^4, Z^5 or Z^6 is N, and b) at least one of Z^3, Z^4 or Z^5 is CR^3, CR^4, or CR^5, respectively, and at least one of R^3, R^4, or R^5 is R^U,

each occurrence of R^U is $NRCOR^7$, $CONR(R^7)$, $SO_2NR(R^7)$, $NRSO_2R^7$, $NRCONR(R^7)$, $NRSO_2NR(R^7)$, or $CONRNR(R^7)$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, 1, or 2, Y is a bond or is O, S, NR^9, $-OCH_2-$, $-SCH_2$, $-NR^9CH_2$, $O(CH_2)_2-$, -

$S(CH_2)_2$, or $-NR^9(CH_2)_2$, and R^8 is Ar^2, or R^8 and R^9, taken together with the nitrogen atom, form an optionally substituted 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each occurrence of V is a bond or a saturated or unsaturated C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR;

each occurrence of p is 0 or 1;

each occurrence of R^V is R or Ar^2; and

Ar^2 is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar^2 is optionally substituted with r independent occurrences of $W\text{-}R^W$; wherein r is 0-3, W is a bond or is a C_1-C_6 alkylidene chain wherein up to two non-adjacent methylene units of W are optionally replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR; and each occurrence of R^W is independently selected from R', halogen, NO_2, CN, OR', SR', $N(R')_2$, NR'COR', $NR'CON(R')_2$, $NR'CO_2R'$, COR', CO_2R', OCOR', $CON(R')_2$, $OCON(R')_2$, SOR', SO_2R', $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, COCOR', or $COCH_2COR'$;

provided that:

a) when Z^7 is CH and ring B is phenyl and at least one of R^3 or R^4 is $NHCOR^7$, then R^1 is not phenyl only substituted with two or three occurrences of OR'; and

b) when Z^7 is CH and ring B is phenyl and at least one of R^3 of R^4 is $NHCOR^7$, SO_2R^7, $CONRR^7$, then R^1 is not phenyl only substituted with one occurrence of -$CON(R')_2$ in the para position.

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2-4. (Canceled)

5. (Currently amended) The compound of claim 1, wherein R^1 is an optionally substituted ~~from~~ phenyl, cyclohexyl, or pyridyl group.

6. (Original) The compound of claim 1, wherein R^1 is optionally substituted phenyl.

7. (Original) The compound of claim 1, wherein q is 0, 1, 2, or 3 and each independent occurrence of ZR^Z is C_{1-4}alkyl, $N(R')_2$, OR', SR', $CON(R')_2$, NR'COR', $NR'SO_2R'$, or $SO_2N(R')_2$.

8. (Original) The compound of claim 1, wherein q is 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$.

9. (Original) The compound of claim 1, wherein q is 1, and ZR^Z is in the meta position and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$.

10. (Original) The compound of claim 1, wherein $(T)_mR^X$ and $(U)_nR^Y$ are hydrogen, halogen, NO_2, CN, OR, SR or $N(R)_2$, or C_{1-4}aliphatic optionally substituted with oxo, OR, SR, $N(R)_2$, halogen, NC_2 or CN.

11. (Original) The compound of claim 1, wherein $(T)_mR^X$ and $(U)_nR^Y$ are each independently hydrogen, Me, OH, OMe or $N(R)_2$.

12. (Original) The compound of claim 1, wherein $(T)_mR^X$ and $(U)_nR^Y$ are each hydrogen.

13. (Original) The compound of claim 1, wherein ring B is one of rings **i-xiv:**

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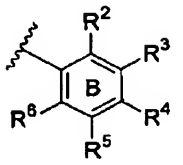
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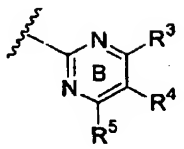
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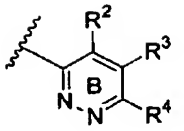
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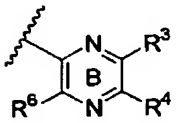
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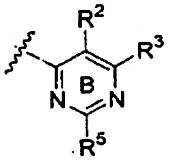
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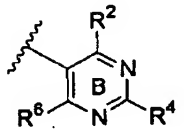
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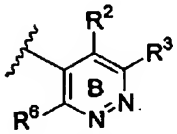
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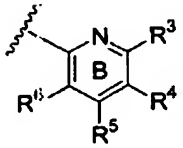
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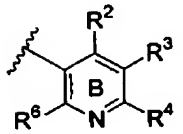
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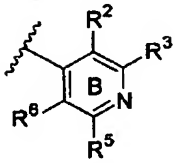
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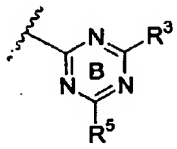
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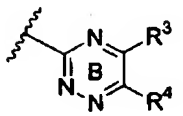
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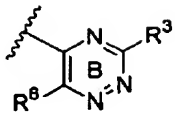
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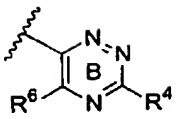
xiv

14. (Original) The compound of claim 1, wherein t is 0, Y is a bond, and R^8 is an optionally substituted aryl or heteroaryl moiety.

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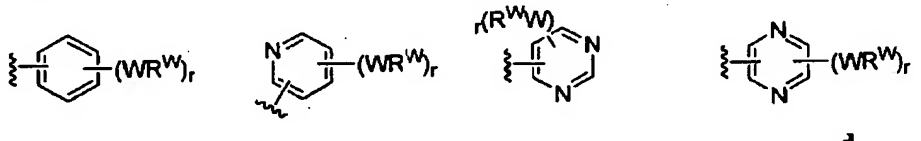
15. (Original) The compound of claim 1, wherein t is 0, Y is a bond, and R^8 is an optionally substituted heteroaryl moiety.

16. (Original) The compound of claim 1, wherein R^7 is $-CH_2-Y-R^8$, and Y is NR^9, O or S, and R^8 is an optionally substituted aryl or heteroaryl moiety.

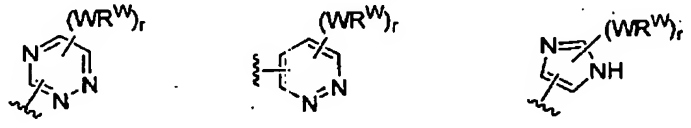
17. (Original) The compound of claim 1, wherein R^7 is $-CH_2-Y-R^8$, and Y is NR^9, O or S, and R^8 is an optionally substituted aryl moiety.

18. (Original) The compound of claim 1, wherein t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur.

19. (Original) The compound of claim 1, wherein R^8 is a 5- or 6-membered aryl or heteroaryl group having one of the formulae:



a b c d



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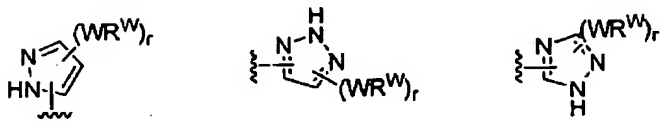

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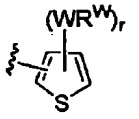

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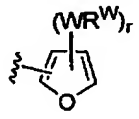

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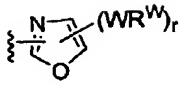

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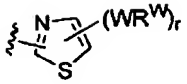

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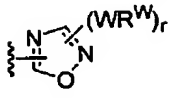

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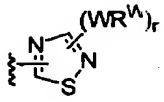

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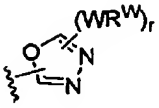

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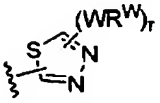
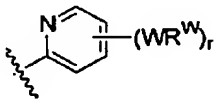
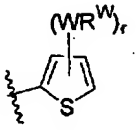


r

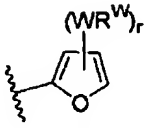
20. (Original) The compound of claim 1, wherein R^8 is a 5- or 6-membered heteroaryl group having one of the formulae:



b-i

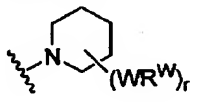


k-i



l-i

21. (Original) The compound of claim 1, wherein R^8 and R^9, taken together, form a group having one of the formulae:



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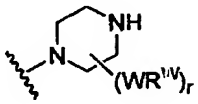

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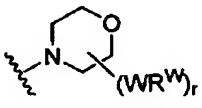

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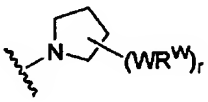

v

22. (Original) The compound of claim 1, wherein r is 0 or 1.

23. (Original) The compound of claim 19, 20, or 21, wherein r is 1, 2, or 3, and each occurrence of halogen, C_{1-4}alkyl, -$(R)_2$, -OR, -SR, -$SO_2N(R)_2$, -$N(R)SO_2R$, -N(R)COR, -$N(R)_2$, -CH_2OR, -$CH_2N(R)_2$, or -CH_2SR.

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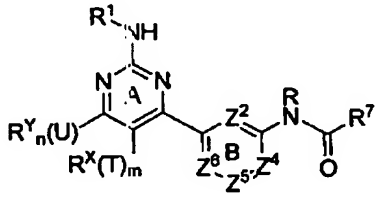
24. (Original) The compound of claim 19, 20, or 21, wherein t is 0, Y is a bond, and R^8 is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**.

25. (Original) The compound of claim 24, wherein R^8 is an optionally substituted heteroaryl group **b-i**, **k-i**, or **l-i**.

26. (Original) The compound of claim 1, wherein t is 1, Y is O, S or NR^9, and R^8 is optionally substituted phenyl.

27. (Original) The compound of claim 1, wherein t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together form an optionally substituted group selected from **s**, **u** or **v**.

28. (Previously presented) The compound of claim 1, wherein Z^3 or Z^5 is CR^3 or CR^5, respectively, and R^3 or R^5 is $NRC(O)R^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR^9, -OCH_2-, -SCH_2, -NR^9CH_2, $O(CH_2)_2$-, -$S(CH_2)_2$, or –$NR^9(CH_2)_2$, and wherein R^8 is Ar^2, or R^8 and R^9, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur, and compounds have the formula **II-A**:



II-A

29. (Previously presented) The compound of claim 28, wherein ring B is selected from **i**, **ii**, **iii**, **iv**, **v**, **vii**, **viii**, **ix**, **x**, **xi**, **xii**, or **xiii** and compounds have one of formulas

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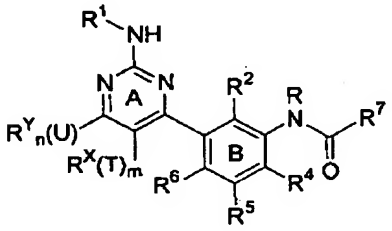
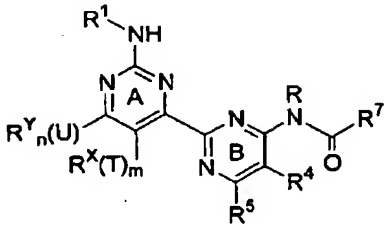
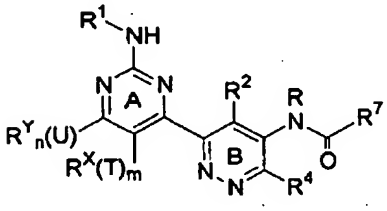
II-A-i, II-A-ii, II-A-iii, II-A-iv, II-A-v, II-A-vii, II-A-viii, II-A-ix, II-A-x, II-A-xi, II-A-xii, or II-A-xiii:



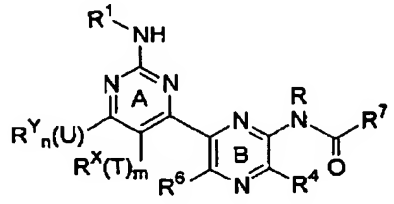
II-A-i



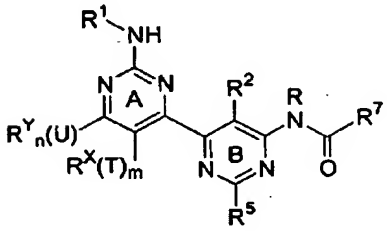
II-A-ii



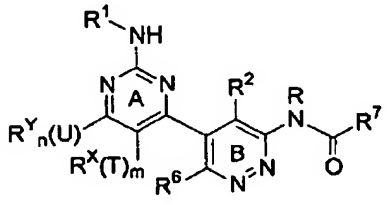
II-A-iii



II-A-iv



II-A-v



II-A-vii

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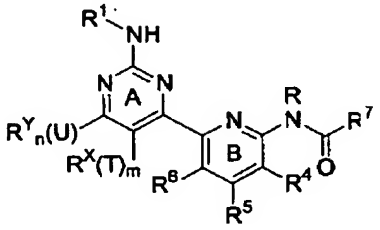
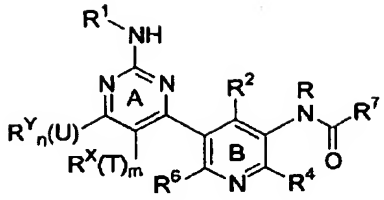
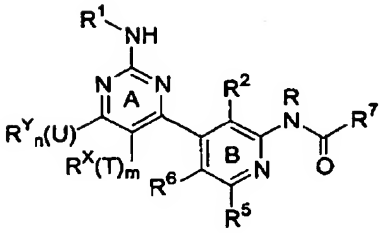


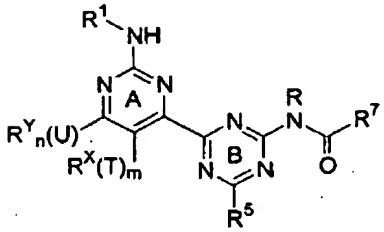
II-A-viii



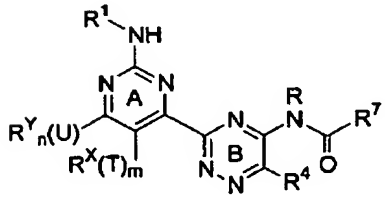
II-A-ix



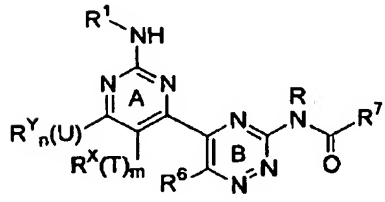
II-A-x



II-A-xi



II-A-xii

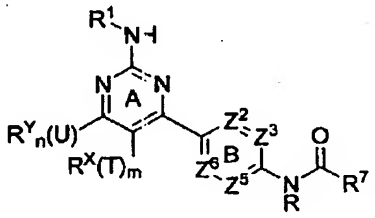


II-A-xiii

30. (Canceled)

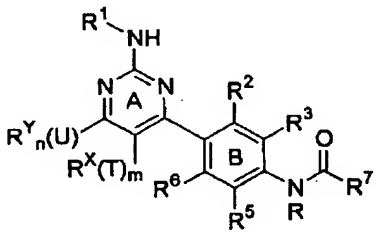
31. (Previously presented) The compound of claim 1, wherein Z^4 is CR^4, and R^4 is $NRC(O)R^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR^9, -OCH_2-, -SCH_2, -NR^9CH_2, $O(CH_2)_2$-, -$S(CH_2)_2$, or –$NR^9(CH_2)_2$, and

wherein R^8 is Ar^2, or R^8 and R^9, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur, and compounds have formula **II-B**:

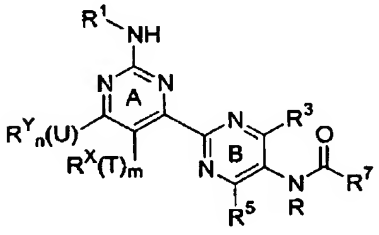


II-B

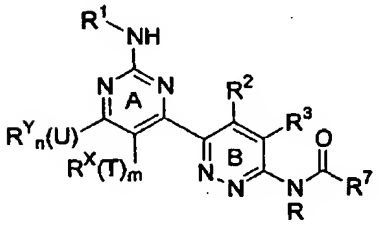
32. (Previously presented) The compound of claim 31, wherein ring B is selected from **i, ii, iii, iv, vi, viii, ix, xii,** or **xiv** and compounds have one of formulas **II-B-i, II-B-ii, II-B-iii, II-B-iv, II-B-vi, II-B-viii, II-B-ix, II-B-xii,** or **II-B-xiv**:



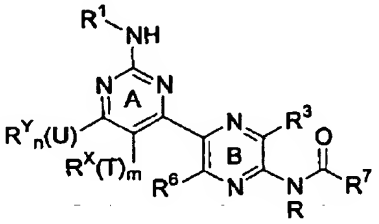
II-B-i



II-B-ii



II-B-iii



II-B-iv

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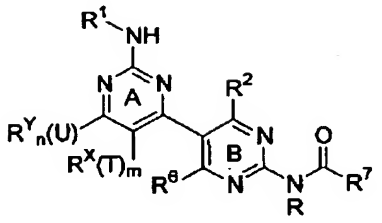
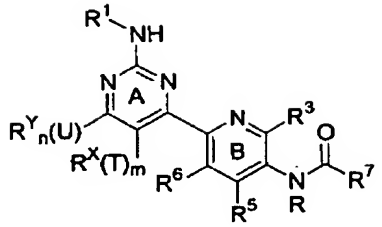
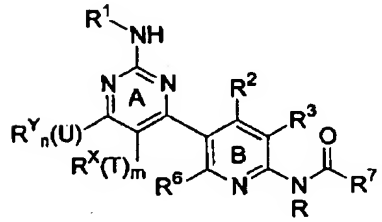


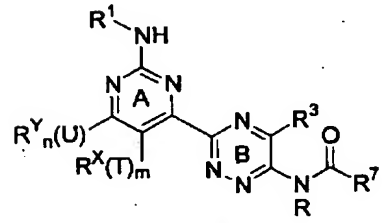
II-B-vi



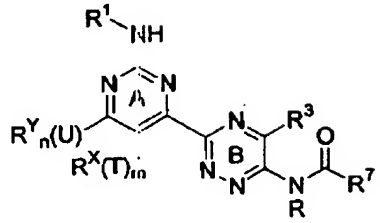
II-B-viii



II-B-ix



II-B-xii

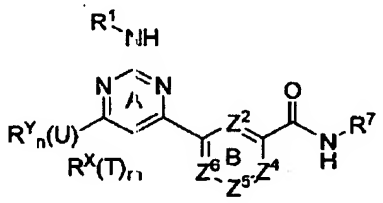


II-B-xiv

33. (Canceled)

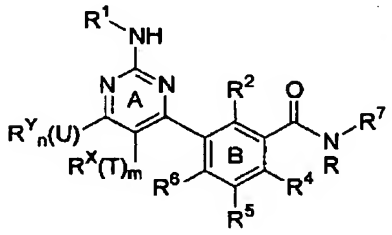
34. (Previously presented) The compound of claim 1, wherein Z^3 or Z^5 is CR^3 or CR^5, respectively, and R^3 or R^5 is $C(O)N(R)(R^7)$, wherein R^7 is $(CH_2)_t$-Y-R^8, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR^9, $-OCH_2-$, $-SCH_2$, $-NR^9CH_2$, $O(CH_2)_2-$, $-S(CH_2)_2$, or $-NR^9(CH_2)_2$, and wherein R^8 is Ar^2, or R^8 and R^9, taken

together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur and compounds have formula **II-C:**

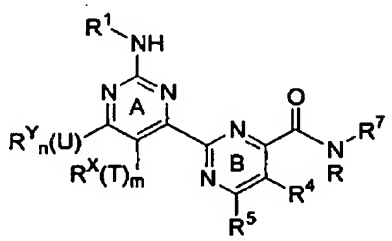


II-C

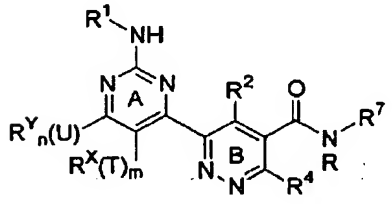
35. (Previously presented) The compound of claim 34, wherein ring B is selected from **i, ii, iii, iv, v, vii, viii, ix, x, xi, xii, or xiii** and compounds have one of formulas **II-C-i, II-C-ii, II-C-iii, II-C-iv, II-C-v, II-C-vii, II-C-viii, II-C-ix, II-C-x, II-C-xi, II-C-xii, or II-C-xiii:**



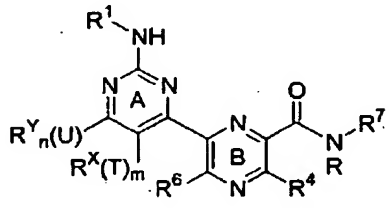
II-C-i



II-C-ii



II-C-iii



II-C-iv

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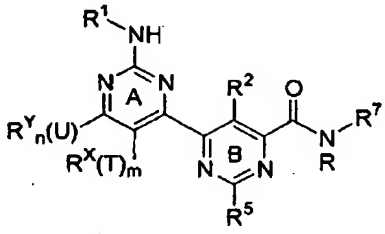
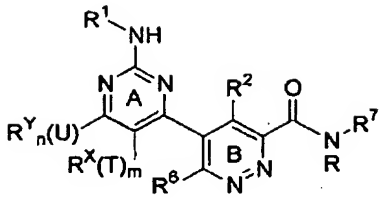
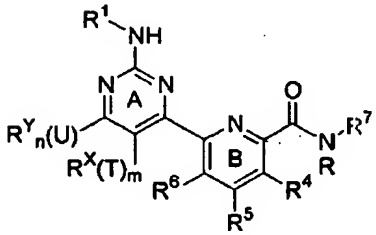


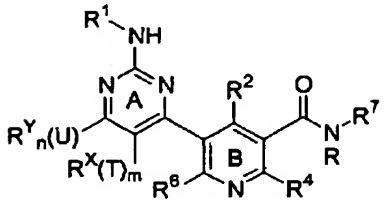
II-C-v



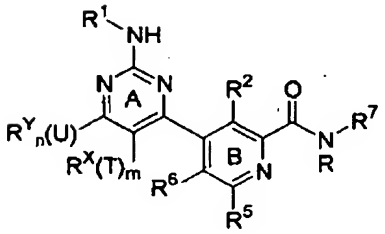
II-C-vii



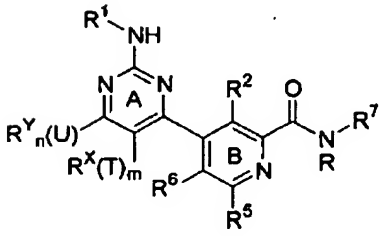
II-C-viii



II-C-ix



II-C-x



II-C-xi

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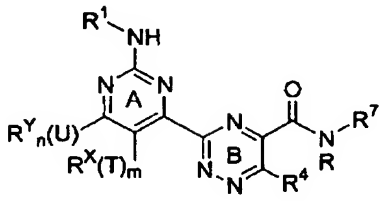
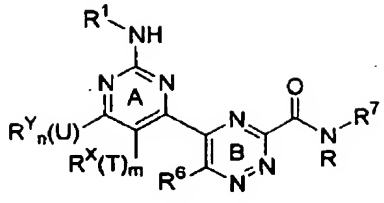


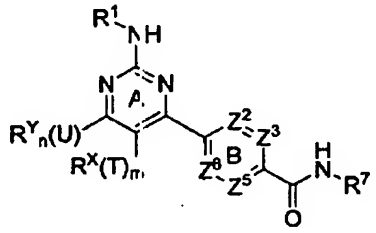
II-C-xii



II-C-xiii

36. (Canceled)

37. (Previously presented) The compound of claim 1, wherein Z^4 is CR^4, and R^4 is $C(O)N(R)(R^7)$, wherein R^7 is $(CH_2)_t$-Y-R^8, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR^9, $-OCH_2-$, $-SCH_2$, $-NR^9CH_2$, $O(CH_2)_2-$, $-S(CH_2)_2$, or $-NR^9(CH_2)_2$, and wherein R^8 is Ar^2, or R^8 and R^9, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur and compounds have formula **II-D:**



II-D

38. (Previously presented) The compound of claim 37, wherein ring B is selected from **i, ii, iii, iv, vi, viii, ix, xii,** or **xiv** and compounds have one of formulas **II-D-i, II-D-ii, II-D-iii, II-D-iv, II-D-vi, II-D-viii, II-D-ix, II-D-xii,** or **II-D-xiv:**

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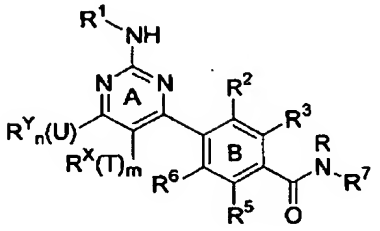
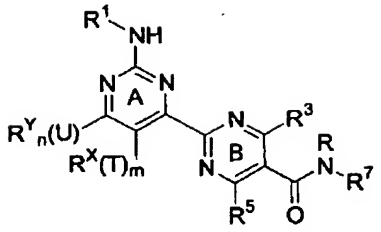
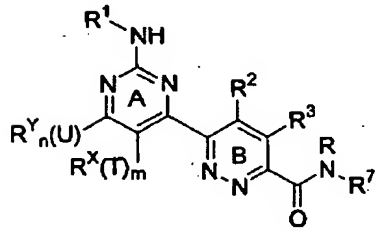


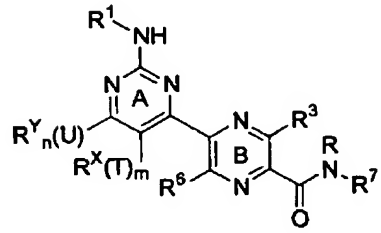
II-D-i



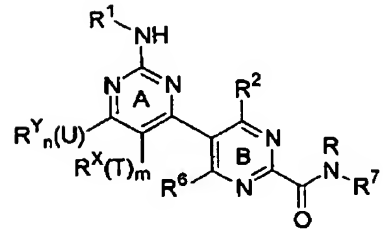
II-D-ii



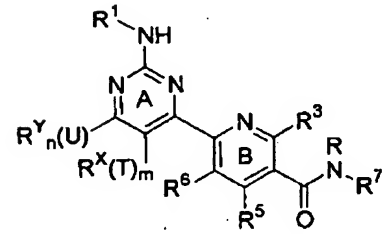
II-D-iii



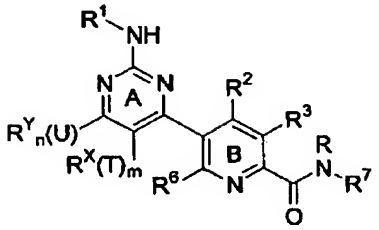
II-D-iv



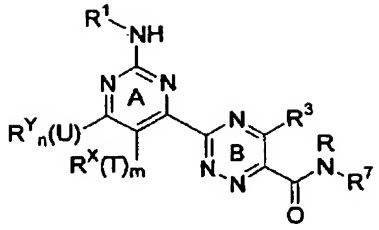
II-D-vi



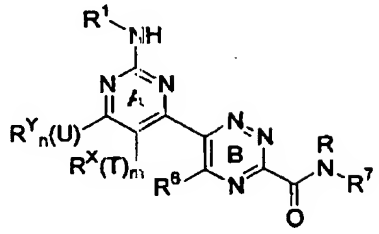
II-D-viii



II-D-ix



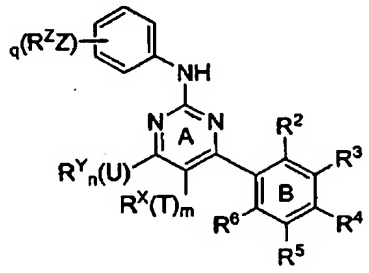
II-D-xii



II-D-xiv

39. (Canceled)

40. (Previously presented) The compound of claim 1, where R^1 is optionally substituted phenyl and ring B is an optionally substituted phenyl group and compounds have the general formula IV:



IV

41. (Previously presented) The compound of claim 40, wherein, R^3 is $NRCOR^7$ and compounds have the general formula IV-A-(i):

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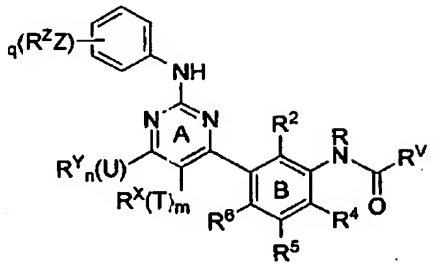
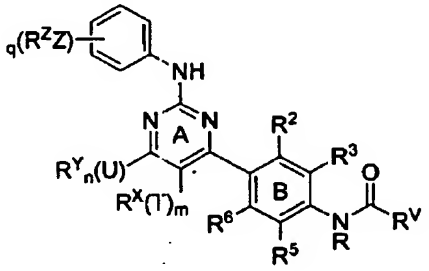


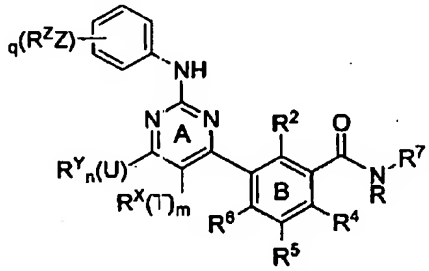
IV-A-(i)

42. (Previously presented) The compound of claim 40, wherein R^4 is $NRCOR^7$ and compounds have the general formula **IV-B-(i):**



IV-B-(i)

43. (Previously presented) The compound of claim 40, wherein R^3 is $CONRR^7$ and compounds have the general formula **IV-C-(i):**



IV-C-(i)

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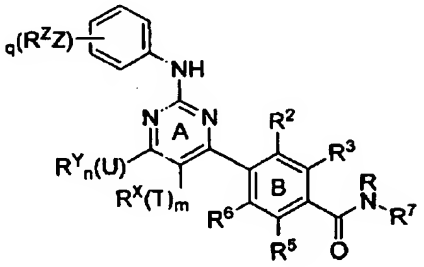
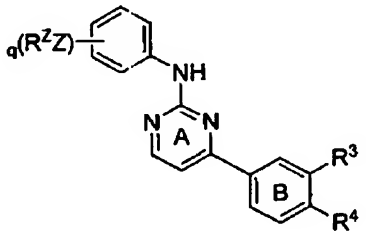
44. (Previously presented) The compound of claim 40, wherein R^4 is $CONRR^7$ and compounds have the general formula **IV-D-(i)**:



IV-D-(i)

45. (Currently amended) The compound of claim 40, wherein R^1 is optionally substituted phenyl, ring A is pyrimidinyl, ring B is phenyl, and R^2, R^5, and R^6 are each hydrogen, and compounds have the general formula**VI**:



VI

46. (Currently amended) The compound of claim 40 or 45, wherein

(a) q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-SO_2NH_2$;

(b) R^3 is $NRCOR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, Y is a bond, and R^8 is phenyl (a), or is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, $-(R)_2$, -OR, -SR, $-SO_2N(R)_2$, $-N(R)SO_2R$, $-N(R)COR$, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and

(c) R^4 is hydrogen.

47. (Previously presented) The compound of claim 40 or 45, wherein:

(a) q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-SO_2NH_2$;

(b) R^3 is $CONRR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, Y is a bond, and R^8 is phenyl (a) or is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, $-(R)_2$, -OR, -SR, $-SO_2N(R)_2$, $-N(R)SO_2R$, -N(R)COR, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and

(c) R^4 is hydrogen.

48. (Previously presented) The compound of claim 40 or 45, wherein:

(a) q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$;

(b) R^4 is $NRCOR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, Y is a bond, and R^8 is phenyl (a) or an optionally substituted heteroaryl moiety selected from one of groups **b** through **z**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, $-(R)_2$, -OR, -SR, $-SO_2N(R)_2$, $-N(R)SO_2R$, -N(R)COR, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and

(c) R^3 is hydrogen.

49. (Previously presented) The compound of claim 40 or 45, wherein:

(a) q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$;

(b) R^4 is $CONRR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, Y is a bond, and R^8 is phenyl (a) or an optionally substituted heteroaryl moiety selected from one of groups **b** through **z**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, $-(R)_2$, -OR, -SR, $-SO_2N(R)_2$, $-N(R)SO_2R$, -N(R)COR, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and

(c) R^3 is hydrogen.

50. (Previously presented) The compound of claim 40 or 45, wherein:

(a) q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$;

(b) R^3 is $NRCOR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, -$(R)_2$, -OR, -SR, -$SO_2N(R)_2$, -$N(R)SO_2R$, -N(R)COR, -$N(R)_2$, -CH_2OR, -$CH_2N(R)_2$, or -CH_2SR; and

(c) R^4 is hydrogen.

51. (Previously presented) The compound of claim 40 or 45, wherein:

(a) q is 0 or 1 and ZR^Z is -NH_2, -OH, C_{1-4}alkoxy, or -$S(O)_2NH_2$;

(b) R^3 is $CONRR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, -$(R)_2$, -OR, -SR, -$SO_2N(R)_2$, -$N(R)SO_2R$, -N(R)COR, -$N(R)_2$, -CH_2OR, -$CH_2N(R)_2$, or -CH_2SR; and

(c) R^4 is hydrogen.

52. (Previously presented) The compound of claim 40 or 45, wherein:

(a) q is 0 or 1 and ZR^Z is -NH_2, -OH, C_{1-4}alkoxy, or -$S(O)_2NH_2$;

(b) R^4 is $NRCOR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents include halogen, C_{1-4}alkyl, NH_2, OH, SH, SO_2NH_2, C_{1-4}alkoxy, C_{1-4}thioalkyl, CH_2OR, $CH_2N(R)_2$, or CH_2SR; and

(c) R^3 is hydrogen.

53. (Previously presented) The compound of claim 40 or 45, wherein:

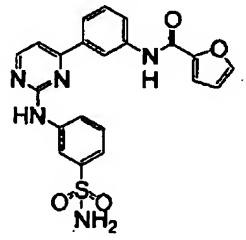
(a) q is 0 or 1 and ZR^Z is -NH_2, -OH, C_{1-4}alkoxy, or -$S(O)_2NH_2$;

(b) R^4 is $CONRR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a group

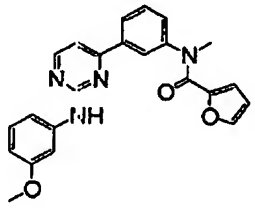
selected from s, t, u, or v, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, $-(R)_2$, -OR, -SR, $-SO_2N(R)_2$, $-N(R)SO_2R$, $-N(R)COR$, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and

(c) R^3 is hydrogen.

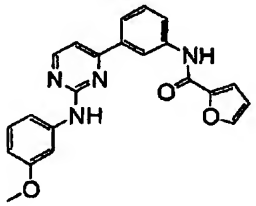
54. (Previously presented) The compound of claim 1, having one of the following structures:



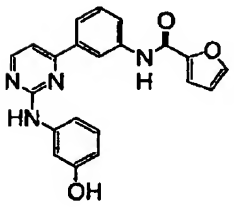
IV-A(i)-1



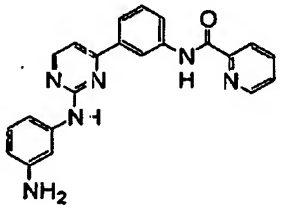
IV-A(i)-2



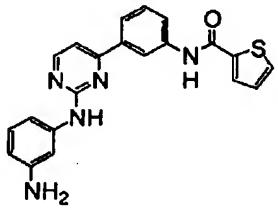
IV-A(i)-3



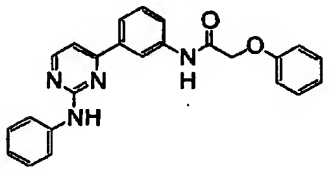
IV-A(i)-4



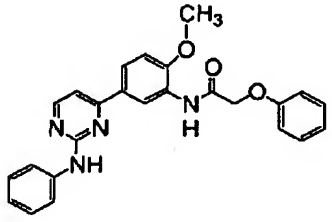
IV-A(i)-5



IV-A(i)-6



IV-A(i)-7



IV-A(i)-8

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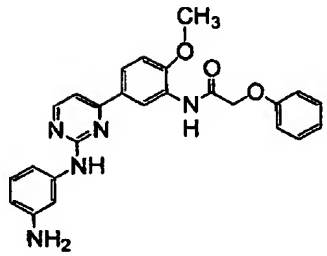
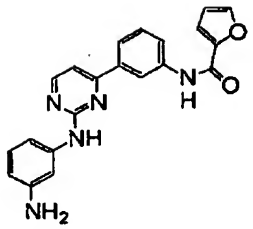
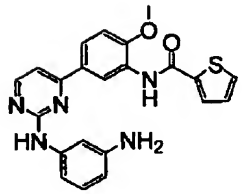


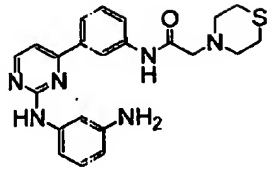
IV-A(i)-9



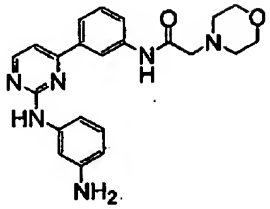
IV-A(i)-10



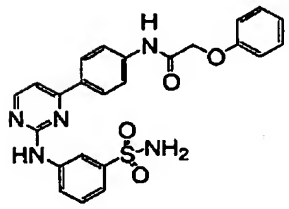
IV-A(i)-11



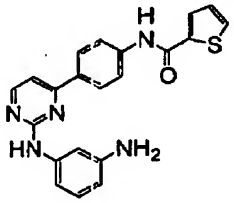
IV-A(i)-12



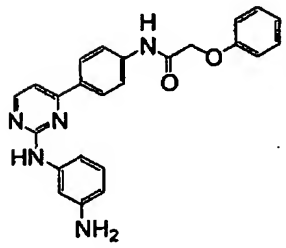
IV-A(i)-13



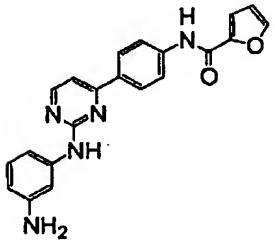
IV-B(i)-1



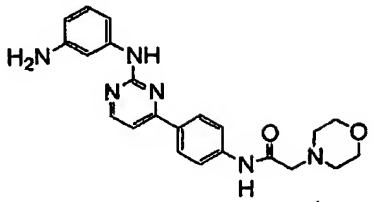
IV-B(i)-2



IV-B(i)-3



IV-B(i)-4



IV-B(i)-5

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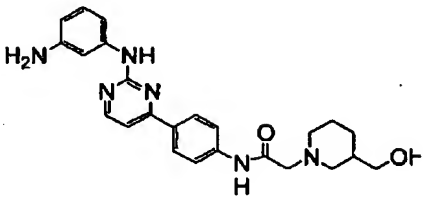
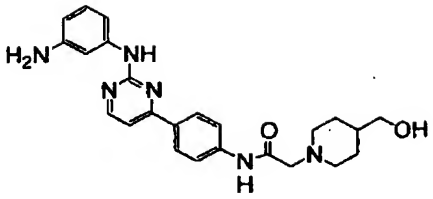
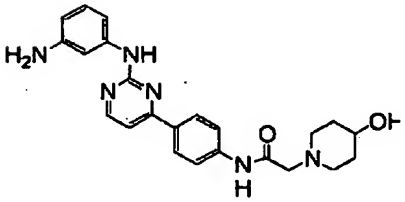


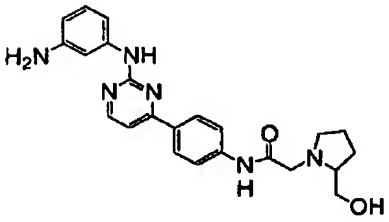
IV-B(i)-6



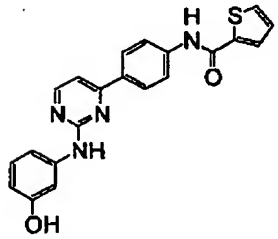
IV-B(i)-7



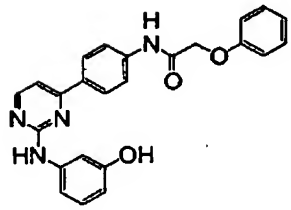
IV-B(i)-8



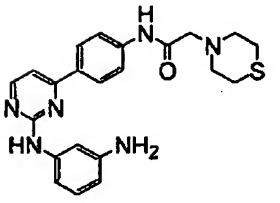
IV-B(i)-9



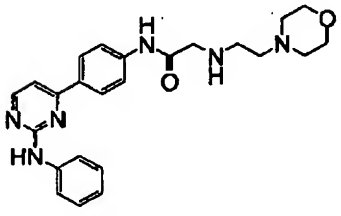
IV-B(i)-10



IV-B(i)-11



IV-B(i)-12



IV-B(i)-13

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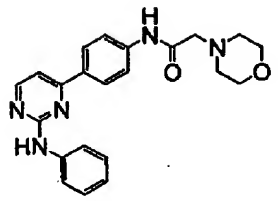
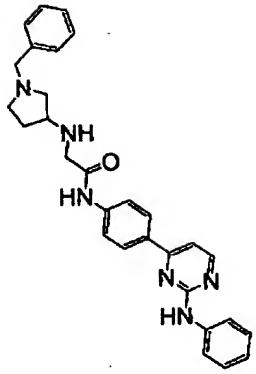
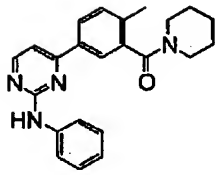


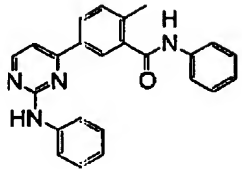
IV-B(i)-14



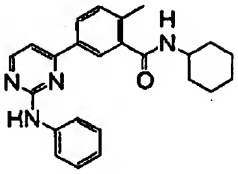
IV-B(i)-15



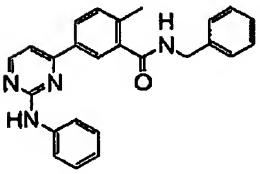
IV-C(i)-1



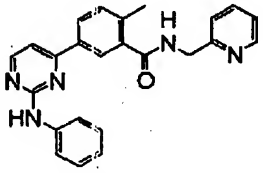
IV-C(i)-2



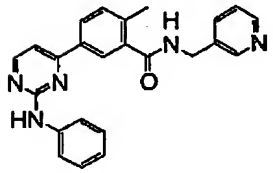
IV-C(i)-3



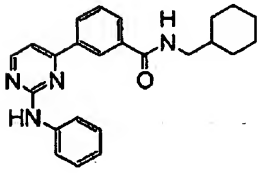
IV-C(i)-4



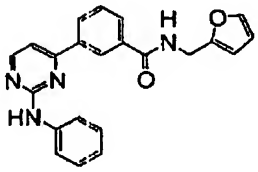
IV-C(i)-5



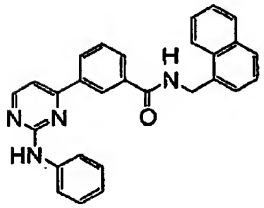
IV-C(i)-6



IV-C(i)-7



IV-C(i)-8



IV-C(i)-9

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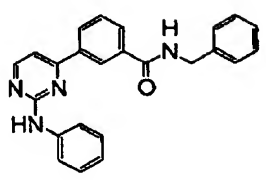
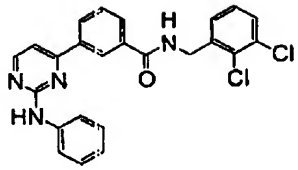
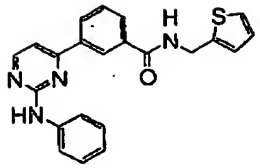


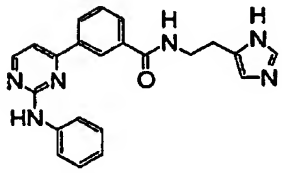
IV-C(i)-10



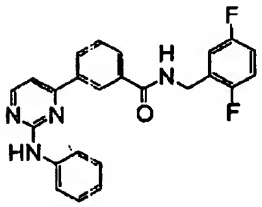
IV-C(i)-11



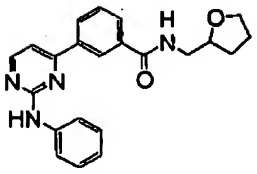
IV-C(i)-12



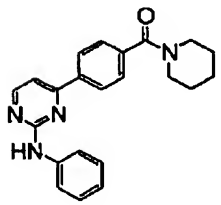
IV-C(i)-13



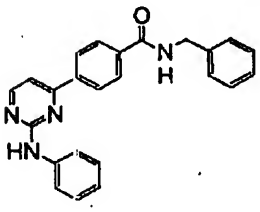
IV-C(i)-14



IV-C(i)-15



IV-D(i)-1



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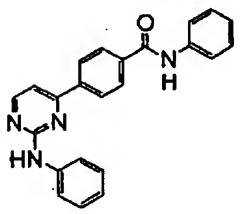

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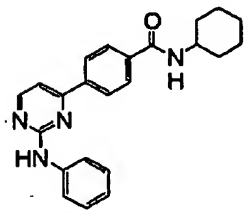

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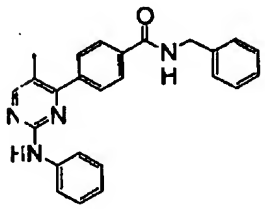
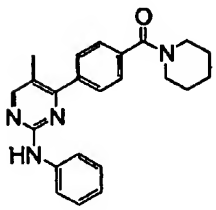


IV-D(i)-5



IV-D(i)-6

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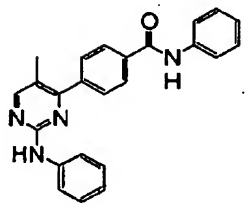
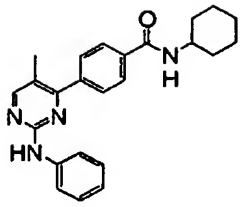


IV-D(i)-7



IV-D(i)-8

55. (Original) A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

56. (Currently amended) The composition of claim 55, further comprising an additional therapeutic agent selected from ~~a chemotherapeutic or anti-proliferative agent,~~ a treatment for Alzheimer's Disease, ~~a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS),~~ a treatment for asthma, ~~an agent for treating schizophrenia,~~ an anti-inflammatory agent [[,]] or an immunomodulatory or immunosuppressive agent, ~~a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an agent for treating a blood disorder, or an agent for treating an immunodeficiency disorder~~.

57. (Currently amended) A method of inhibiting JAK kinase activity in a biological sample *in vitro* ~~or a patient~~, comprising the step of contacting said biological sample ~~or patient~~ with:

a) the composition of claim 55; or

b) the compound of claim 1.

58. (Currently amended) A method of treating or lessening the severity of a disease or disorder selected from rheumatoid arthritis, allergic or type I hypersensitivity reaction, asthma, familial amyotrophic lateral sclerosis (FALS) or

transplant rejection, ~~an immune response, an autoimmune disease, a neurodegenerative disorder, or a solid or hematologic malignancy~~ comprising administering to a patient in need thereof a compound of claim 1 or a composition of claim 55.

59. (Canceled)